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Learning Series - #21

Making sense of FibroScan (liver elastrography) and liver fibrosis/damage

Liver fibrosis is a major cause of morbidity and mortality worldwide due to chronic viral hepatitis and, more recently, from fatty liver disease associated with obesity. It can result from different underlying chronic liver diseases, such as chronic viral infection, excessive alcohol consumption, fatty liver disease or autoimmune liver diseases. While fibrosis is reversible in its initial stages, progressive fibrosis can lead to cirrhosis.

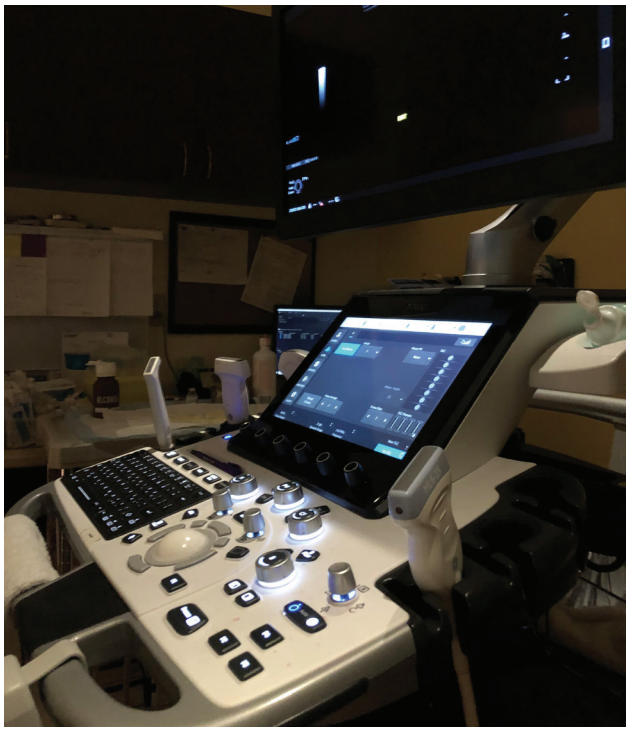
The development of liver cirrhosis is driven by several different risk factors, the frequency of which varies regionally. Thus, in western countries excessive alcohol consumption, hepatitis C virus (HCV) infection and fatty liver disease are most common, whereas chronic hepatitis B virus (HBV) infection is the main risk factor in Asia. Furthermore, liver cirrhosis can evolve from a chronic immune-mediated damage in the context of autoimmune liver disease (AILD), such as primary sclerosing cholangitis (PSC), primary biliary cholangitis (PBC) and autoimmune hepatitis (AIH). Other less common risk factors include Wilson's disease (copper overload), haemochromatosis (iron overload) and α1-antitrypsin deficiency, while some cases are cryptogenic (due to unidentified causes). Increasing evidence suggests that even early stages of cirrhosis may be reversible.

FibroScan is a non-invasive ultrasound-based diagnosis technique (elastography) that helps assess the health of the liver. It measures fibrosis (scarring or thickening of tissues) and steatosis (fatty change). For some patients, it can replace a liver biopsy.

Fibroscan can also be used for pediatric patients as fatty liver disease is a growing problem among children due to poor diet and lack of exercise.

FibroScan test may be recommended for the following chronic liver conditions:

- Autoimmune Hepatitis
- Cirrhosis
- Genetic Diseases (such as Hemochromatosis and Wilson's Disease)
- Hepatitis B
- Hepatitis C
- Alcoholic Liver Disease
- Non-Alcoholic Steatohepatitis (NASH)



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Making sense of FibroScan (liver elastrography) and liver fibrosis/damage (cont'd)

Understanding FibroScan results

a. CAP score is a measurement of fatty change in the liver and it's used to find out the steatosis grade.

CAP Score	Steatosis Grade	Amount of Liver with Fatty Change
238 to 260 dB/m	S1	11% to 33%
260 to 290 dB/m	S2	34% to 66%
> 290 dB/m	S3	≥67%

b. FibroScan measures scarring by measuring the stiffness of the liver.

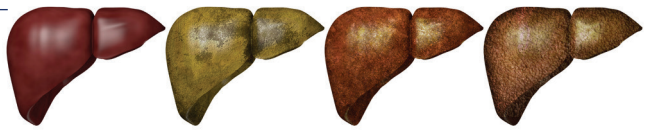
FibroScan fibrosis result along with the patient's medical history are used to determine the fibrosis score.

- **Fibrosis score F0 to F1:** No liver scarring or mild liver scarring
- **Fibrosis score F2:** Moderate liver scarring
- **Fibrosis score F3:** Severe liver scarring
- **Fibrosis score F4:** Advanced liver scarring (cirrhosis)

The table below shows liver diseases, ranges of fibrosis results, and the matching fibrosis score. The ranges of fibrosis results in the table are estimates.

Liver diseases	F0 to F1	F2	F3	F4
Hepatitis B	2 -7 kPa	8- 9 kPa	8- 11 kPa	≥18 kPa
Hepatitis C	2- 7 kPa	8- 9 kPa	9- 14 kPa	≥14 kPa
HIV/HCV coinfection	2- 7 kPa	7- 11 kPa	11- 14 kPa	≥14 kPa
Cholestatic Disease	2 -7 kPa	7- 9 kPa	9- 17 kPa	≥17 kPa
Non-Alcoholic Fatty Liver Disease (NAFLD or NASH)	2 -7 kPa	7.5- 10 kPa	10- 14 kPa	≥14 kPa
Alcohol Liver Disease (ALD)	2 -7 kPa	7- 11 kPa	11- 19 kPa	≥19 kPa

Stages of liver damage



Underwriting considerations

1. Liver stiffness can be impacted by:
   a. the etiology of the chronic liver disease. For each stage of fibrosis, cutoffs are higher than in chronic viral hepatitis either because of the nature of the liver disease or because of cholestasis. Similar, higher cutoffs for each fibrosis stage were described in alcoholic liver disease
   b. The non-fasting status, flare of transaminases, heart failure, extrahepatic cholestasis, and presence of severe steatosis. In addition, interobserver variability can also impact on management of patients with chronic liver diseases.
2. Fibrosis result may be overestimated (liver may have less scarring than what the fibrosis result says) if the patient has:
   a. Liver inflammation (caused by a recent liver illness or drinking alcohol).
   b. Benign or cancerous tumors of the liver.
   c. Liver congestion (usually caused by heart failure).
3. FibroScan results may also be less accurate if the patient has:
   a.BMI >30
   b. Ascites
   c. Biliary obstruction
4. The correct classification of fibrosis stage might impact the access to new direct-acting antiviral (DAA) treatment for patients with chronic hepatitis C (CHC) or the duration of treatment
5. There is no evidence that presence of hepatocellular carcinoma might impact on liver stiffness. However, the FibroScan has a prognostic value to predict the development of liver neoplasm.